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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/220,920 | 12/24/98 | MILBRANDT J | 6029-7996 |

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| MURPHY, J | |
| ART UNIT | PAPER NUMBER |
| 1646 | 16 |

DATE MAILED: 04/10/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/220,920 | MILBRANDT ET AL. | |
| | Examiner | Art Unit | |
| | Joseph F Murphy | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 February 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1, 11-12,15-27,39 and 40* is/are pending in the application.

4a) Of the above claim(s) *1 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,15-27,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

## DETAILED ACTION

### *Continued Prosecution Application*

The request filed on 2/1/2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09220920 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 12, 15-18, 25, 27, 39 were amended, and new claim 40 was added, in paper No. 15, 2/1/2001. Claims 1 and 11 stand withdrawn from consideration as being drawn to a non-elected invention pursuant to 37 CFR 1.142(b).

Claims 12, 15-27, 39-40 are pending and under consideration.

### *Response to Amendment*

The rejection of claims 17 and 18 under 35 USC 112, first paragraph for recitation of the term "complement" has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 12 and 15 under 35 USC 112, second paragraph for recitation of the term "about" has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 16-18 under 35 USC 112, second paragraph for recitation of the term "specifically hybridize" has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 12, 15-16, 19-27 and 39 under 35 USC 112, first paragraph as lacking written description of "conservatively substituted variants", has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 12 and 15-16 under 35 USC 102(a) has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claims 19 and 20 under 35 USC 103(a) has been obviated by Applicant's amendment, and is thus withdrawn.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 12, 25 and 39 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, i.e. a product of nature.

The instant claims are drawn to a polynucleotide encoding a naturally occurring artemin amino acid sequence. As written, the claims read on whole, naturally-occurring polynucleotides. Amending the claim to encompass an isolated polynucleotide that does not occur in nature would obviate this rejection.

### *Claim Rejections - 35 USC § 112 first paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 15-26, 39-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding an amino acid sequence set

forth in SEQ ID NO: 26, does not reasonably provide enablement for amino acid sequences that are fragments of said sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 12, 15 and 25 are overly broad in the recitation of "fragments". There is not adequate guidance as to the nature of the fragments which Applicants claim. The claim can be reasonably interpreted to include any polynucleotide that encodes any polypeptide that is smaller in size than the polypeptide of SEQ ID NO: 26. There is no guidance provided in the specification as to the relationship between the structure of artemin and its function. Without this information, it would require undue experimentation for one of skill in the art to generate a polynucleotide encoding an artemin polypeptide, other than that which is exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 12 and 15 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification

and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 16-26, 39-40 are rejected insofar as they depend on the recitation in claims 12, 15 and 25 of "fragment" of a polynucleotide encoding an amino acid sequence set forth in SEQ ID NO: 26

Claims 12, 15-27, 39-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding an amino acid sequence set forth in SEQ ID NO: 26, does not reasonably provide enablement for amino acid sequences that are, for a polynucleotides encoding amino acid sequences that have at least 65% amino acid sequence identity to SEQ ID NO: 26. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 12, 15, 25 and 27 are overly broad in the recitation of "is at least 65% identical" since no guidance is provided as to which of the myriad of polynucleotide species encode polypeptide species encompassed by the claim will retain the characteristics of an artemin polypeptide. The specification (page 20, lines 27-30), Applicants disclose that the artemin polypeptide can also include modifications of the artemin sequences including sequences in which one or more amino acid have been inserted, deleted or replaced with a different amino acid, without disclosing any actual or prophetic examples on expected performance parameters of any of the possible muteins of artemin. However, it is known in the art that even single amino

acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding an artemin polypeptide other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of

direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 12, 15, 25 and 27 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 16-24, 26 and 39-40 are rejected insofar as they depend on the recitation in claims 12, 15, 25 and 27 of a polynucleotide encoding an amino acid sequence "65% identical" to an amino acid set forth in SEQ ID NO: 26

Claims 12, 15-27, 39-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 12, 15, 25 and 27 encompasses a nucleic acid sequence encoding an amino acid which is at least 65% identical to SEQ ID NO: 26. The specification provides adequate guidance for polynucleotides encoding SEQ ID NO: 26 and use of these to make the encoded protein, however the specification fails to provide adequate guidance on which of the nucleic acid sequences encompassed by the claim can be made and used to promote survival of neurons. The relationship between the structure of the polynucleotide encoding the amino acid sequence is not correlated to the function of the encoded amino acid sequence.

In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. In the instant case there are a large number of nucleic acid sequences which encode amino acid sequences 'at least 65% identical to SEQ ID NO: 26', however these sequences encode various unrelated proteins. Therefore, while the specification provides the necessary guidance to make the polynucleotides encoding SEQ ID NO: 26, it does not provide the necessary guidance for one of skill in the art to make and use the nucleic acid sequences which do not encode an artemin polypeptide.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time the invention was made, it would have required one of skill in the art undue experimentation to make and use the invention as claimed.

***Claim Rejections - 35 USC § 112 second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12, 15-26, 39-40 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12, 15 and 25 are indefinite in the recitation of the term "fragments". This language is vague and indefinite since it encompasses potentially any portion of the polypeptide including a single amino acid. There is no guidance provided as to what specific sequences the term "fragment" refers to. Therefore, the metes and bounds of the claim are unclear. Claims 16-26, 39-40 are vague and indefinite insofar as they depend on claims 12, 15 and 25 for the recitation of "fragment".

***Conclusion***

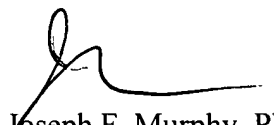
No claim is allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



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Patent Examiner
Art Unit 1646
April 5, 2001

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PRIMARY EXAMINER